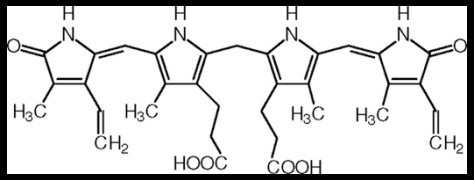

Neonatal Jaundice Hyperbilirubinemia

Abdulrahman Al Nemri, MD
Professor of Pediatric
Consultant Neonatologist

Dr. notes
kaplan
+
illustrated book

Undergraduate Slide

AbdulRahman Alnemri, MD
Professor of pediatric
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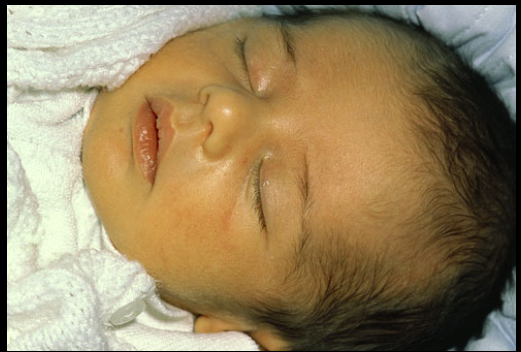
100 $ questions on Neonatal Jaundice (NJ)

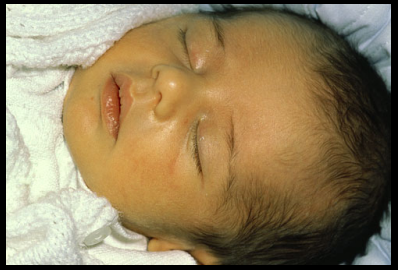
1. What is the commonest cause of neonatal J ? Physiologic
2. What is the frequently used therapy for neonatal J ?
3. Why do we need to study Neonatal J ?

The baby have 80% chance to develop jaundice, and if not properly treated and diagnosed , then life threatening complications might happen



Monday, February 10, 2020

Introduction



- Yellow-orange pigment (icterus-bilirubin) in the skin and sclera
- It is one of the most common clinical phenomena encountered in newborns (How common is it?)
- It may be a sign of another illness
- It is the cause of one catastrophic complication kernicterus

Clinical Physiology

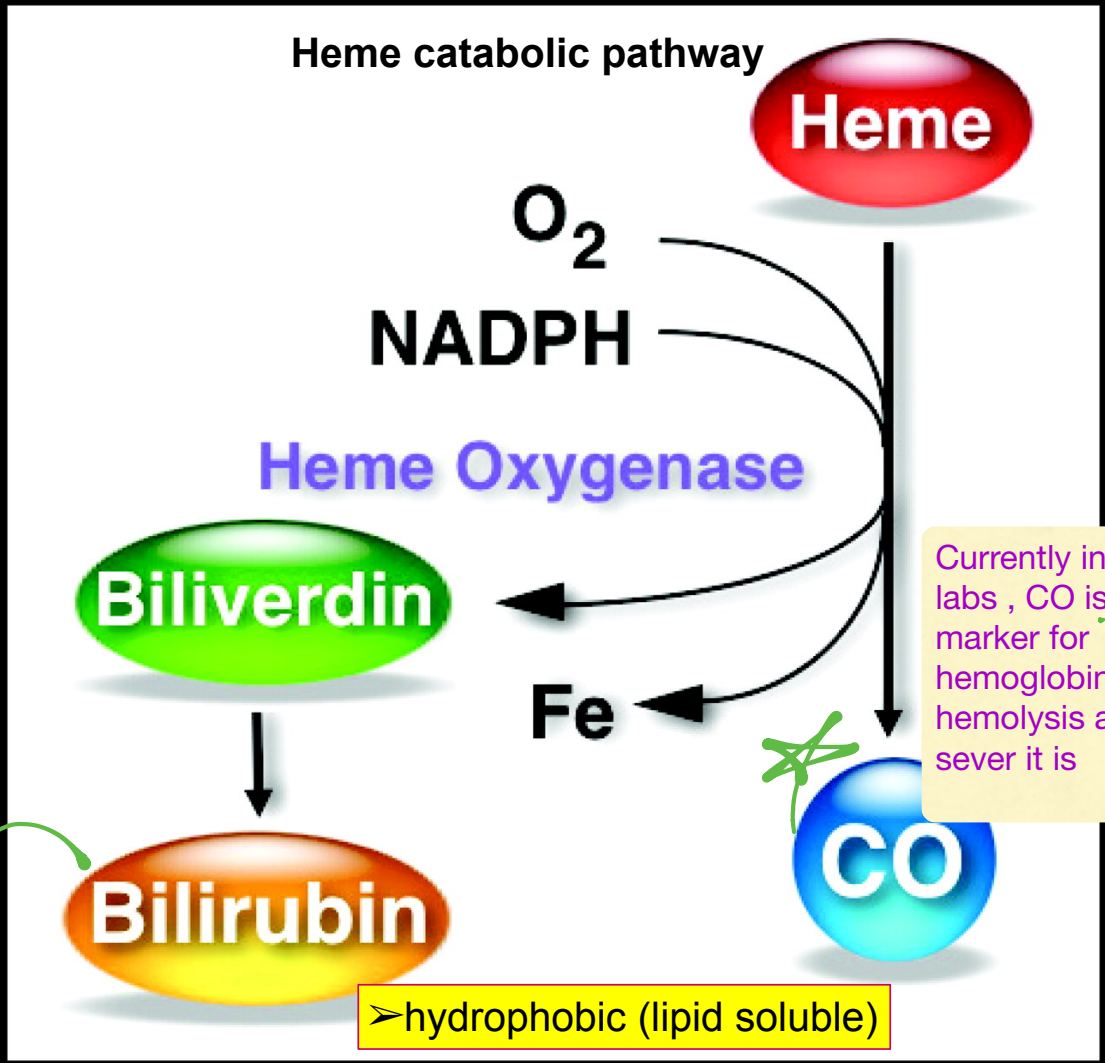
1- Bilirubin Production

➢ ***What is (are) the source(s) of Bilirubin ?***

1. Degrading heme from hemoglobin-containing RBCs (80%)
2. 20% from ineffective erythropoiesis
3. Turnover of other hemoproteins (e.g., myoglobin, catalase, nitric oxide synthase, peroxidases, and cytochromes).

So:

Heme → (Heme oxygenase) Biliverdin → (Biliverdin Reductase) bilirubin



Currently in some labs , CO is used as a marker for hemoglobinopathies/ hemolysis and how sever it is

Hydrophobic , lipid soluble , that's why it's dangerous , may pass through BBB

Wong, R. J. et al. Neoreviews 2007;8:e58-e67

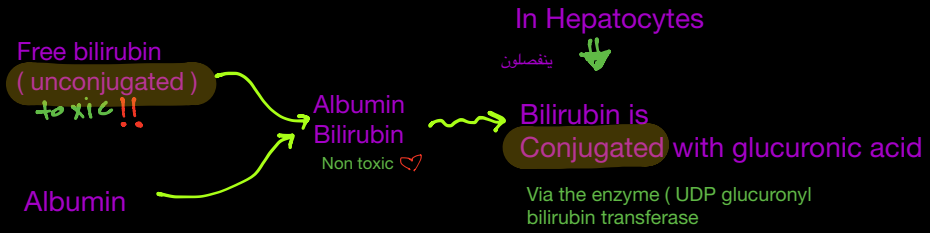
2- Bilirubin Transport

- It binds reversibly to albumin (bilirubin:albumin) → As a protective mechanism, binding to albumin will make it larger complex

  (about 0.8 - 7 mg of bilirubin per gram of albumin)

this ratio is imp for physician

- Low Albumin level and affinity binding sites
- Free" bilirubin is hydrophobic (lipid soluble)
- The movement of bilirubin from the circulation into tissue cross blood brain brayer



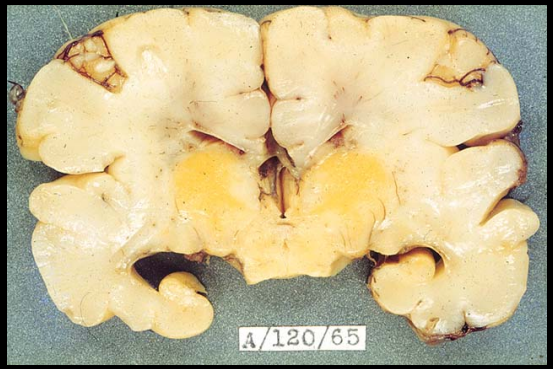
The very rare Crigler–Najjar syndrome, in which the enzyme glucuronyl transferase is deficient or absent, may result in extremely high levels of unconjugated bilirubin.

basal ganglia

hippocampus

Kernicterus

geniculate bodies



cranial nerve nuclei

Commonly the auditory nerve (MCQs)

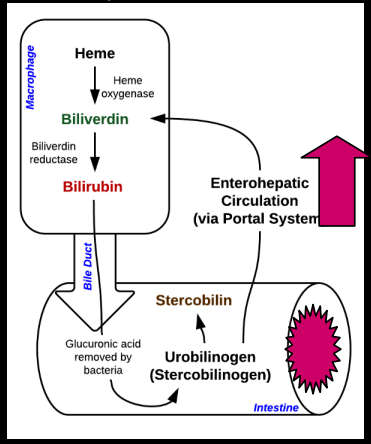
3- Conjugation

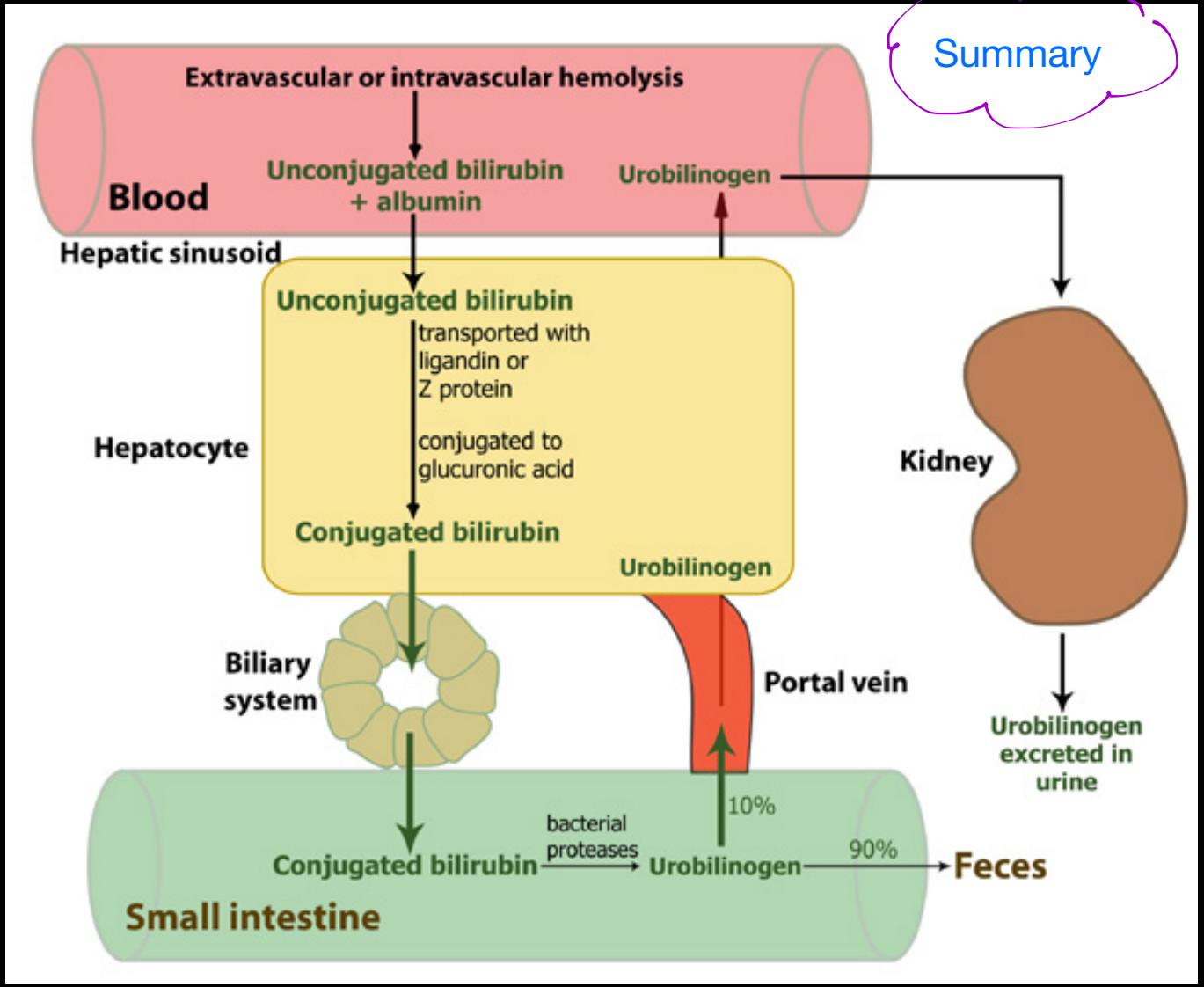
- Conjugation of bilirubin with glucuronic acid (water-soluble, non-neurotoxic bilirubin)
- ***Uridine diphospho - Glucuronosyl Transferase (UDGT)***
- Slower rate of hepatic uptake of free bilirubin from the blood
- Decreased concentrations and activity ***of (UDGT)*** ***?***

4- Bilirubin Excretion

- Conjugated bilirubin enter the bile ducts and are excreted with the bile into the intestinal tract.
- Mono or Diglucuronide → unconjugated Bili
- In the colon, bacterial flora in older neonates hydrogenate bilirubin → urobilinogen, urobilins, and stercobilins (stool color)

Mcq:
Intestinal obstruction = excessive entero- hepatic circulation = jaundice




Summary
Extravascular or intravascular hemolysis
Blood
Unconjugated bilirubin
+ albumin
Urobilinogen
Hepatic sinusoid
Unconjugated bilirubin
transported with
ligandin or
Z protein
Hepatocyte
conjugated to
glucuronic acid
Conjugated bilirubin
Urobilinogen
Kidney
Biliary
system
Portal vein
Urobilinogen
excreted in
urine
10%
bacterial
proteases
Conjugated bilirubin
Urobilinogen
90%
Feces
Small intestine

Etiological Classification

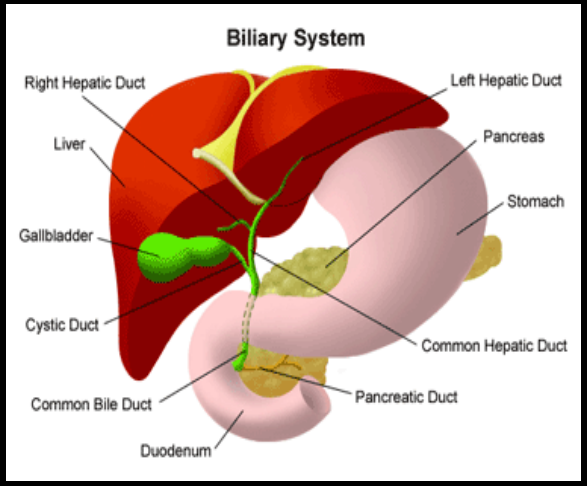
Excessive production
Problem with conjugation
Decreased elimination

Bilirubin production

Binding

Transportation

Entero-hepatic conjugation



Hour-specific Bilirubin load

Bilirubin Elimination

Etiology :

1- excessive production

- hemolysis → blood group incompatibility
  Early Jaundice
  - 2 major
    - RH incompatibility (Rhesus) — now rare but still seen, small table
      - Scenario:
        - * the mother is negative
        - * baby is positive
        - * mother has anti D
        - * second pregnancy will cause hemolysis mostly
    - ABO incompatibility "more common"
      - Scenario
        - * O mother has anti A and anti B
        - * baby either A or B
        - = small amount of antibodies will cross placenta and cause hemolysis
  - 1 minor ??
- G6PD deficiency

Q: why SCD won't cause hemolysis in neonates ?? Because they have HbF

- spherocytosis
- destruction of RBCs from other antibodies (when mother has connective tissue disease ex:SLE)
- Cephalic hematoma will be extravascular hemolysis
- Or when baby has polycythemia (excessive hg = excessive bilirubin)

Criteria of PHYSIOLOGIC jaundice ? MCQS AND OSCE

1- by exclusion

2- after 24 hours NOT BEFORE

3- normal stool and urine
4- baby is fine , asymptotic and active
5- the INDIRECT bilirubin is usually high NOT the direct
6- rate < 5mg/dl/d
7- level < 300 mg/dl

Kaplan

Physiologic Jaundice	Pathologic Jaundice
Appears on second to third day of life (term)	May appear in first 24 hours of life
Disappears by fifth day of life (term)—7th	Variable
Peaks at second to third day of life	Variable
Peak bilirubin <13 mg/dL (term)	Unlimited
Rate of bilirubin rise <5 mg/dL/d	Usually >5 mg/dL/d

Table 1-6. Physiologic Jaundice Versus Pathologic Jaundice

illustrated book of pediatrics

Jaundice starting at <24 h of age	*Haemolytic disorders*:
	Rhesus incompatibility
	ABO incompatibility
	G6PD deficiency
	Spherocytosis, pyruvate kinase deficiency
	Congenital infection
Jaundice at 24 h to 2 weeks of age	Physiological jaundice
	Breast milk jaundice
	Infection, e.g. urinary tract infection
	Haemolysis, e.g. G6PD deficiency, ABO incompatibility
	Bruising
	Polycythaemia
	Crigler–Najjar syndrome
Jaundice at >2 weeks of age	*Unconjugated:*
	Physiological or breast milk jaundice
	Infection (particularly urinary tract)
	Hypothyroidism
	Haemolytic anaemia, e.g. G6PD deficiency
	High gastrointestinal obstruction, e.g. pyloric stenosis
	Conjugated (>25 µmol/L):
	Bile duct obstruction
	Neonatal hepatitis

2- problem with conjugation

INDIRECT hyperbilirubinemia

- gilbert syndrome (very mild , asymptomatic , usually in adultsb, you do LFT and you find the indirect bilirubin is hight)
- crigler najjar syndrome (common cause of kernicterus in KSA)

DIRECT HYPERBILIRUBINEMIA

- Dubin johnson syndrome
- Rotor syndrome
- Dr note : عشان ما تنسوها مجموعه في قولك ductor ، الدال من دايركت

COMMONEST CAUSE OF KERNICTERUS IN SAUDI ARABIA :
crigler najjar syndrome and G6PD deficiency

Other causes of jaundice :

Breast milk jaundice : occurs early .

Breastfeeding jaundice : decreased intake of breast milk —> dehydrated

Kaplan's

BREAST-FEEDING JAUNDICE VERSUS BREAST-MILK JAUNDICE

Breast-feeding jaundice means a baby is not nursing well and so not getting many calories. This is common in first-time breast-feeding mothers. The infant may become dehydrated; however, it is lack of calories that causes the jaundice. Treatment is to obtain a lactation consultation and rehydrate the baby. The jaundice occurs in the first days of life.
Breast-milk jaundice occurs due to a glucoronidase present in some breast milk. Infants become jaundiced in week 2 of life. Treatment is phototherapy if needed. Although the bilirubin may rise again, it will not rise to the previous level. The baby may then be safely breast fed. The jaundice will be gone by 2–3 months.

Both are safe not causing kernicterus

3-Obstructive jaundice , usullay late (after 2 weeks)

- biliary atresia
- Mass cause obstruction (hemangioma , choledochal cyst , head of pancrease tumor)

4- hepatocyte injury

- TORCH infection (HBV , CMV , rubella , toxoplasmosis) .
- galactocemia.
- Tyrosinemia.

Kaplan

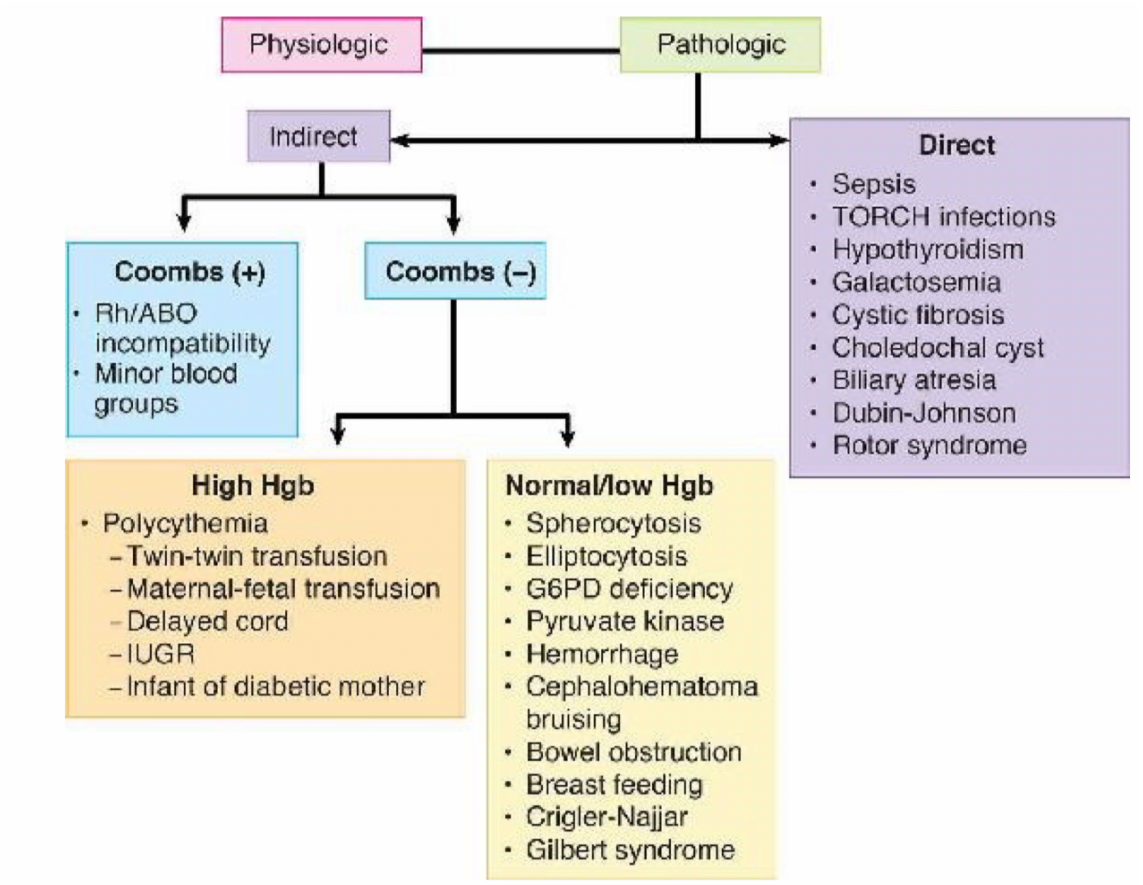
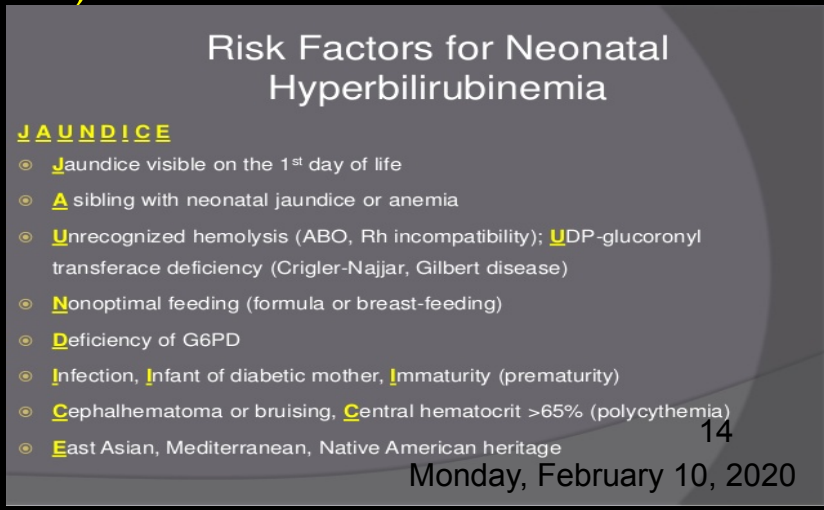


Figure 1-2. Jaundice Workup

What are the risk factors?

- ➢Gestational Age more in premature
- ➢Race (Genetic @ environmental)
- ➢Maternal illness DM & Blood group (ABO or Rhs)
- ➢Family history of jaundice requiring phototherapy
- ➢Hemolysis (G6PD, Spherocytosis)
- ➢Severe bruising
- ➢Breastfeeding



Etiological Classification

- *Increased bilirubin load*

1. ***Haemolytic causes***

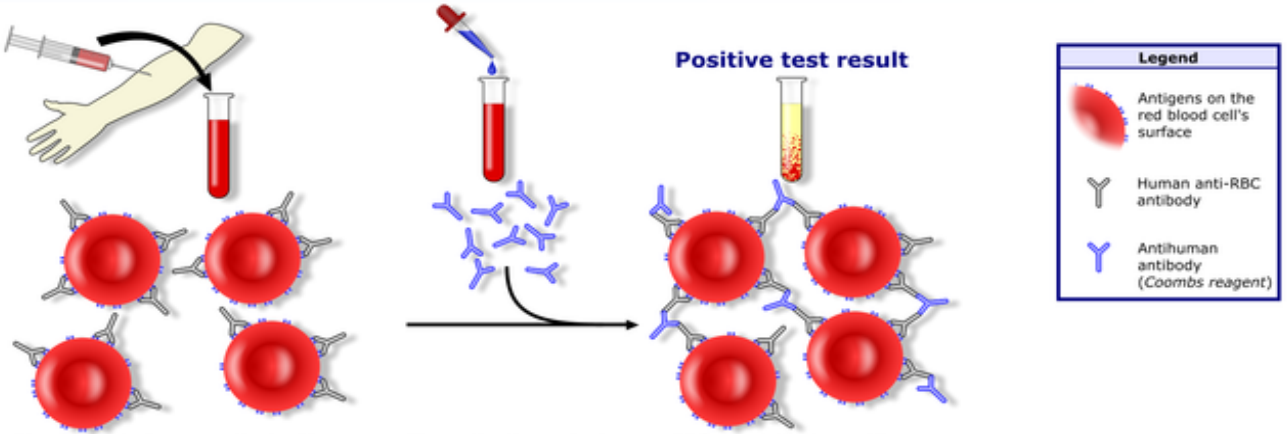
➢Coombs' test positive: Examples ?

➢Coombs' test negative: Examples ?

(red blood cell membrane defects (spherocytosis, elliptocytosis), red blood cell enzyme defects (G6PD deficiency, pyruvate kinase deficiency)

- We do not include thalassemia or SCD. why?

Direct Coombs test / Direct antiglobulin test

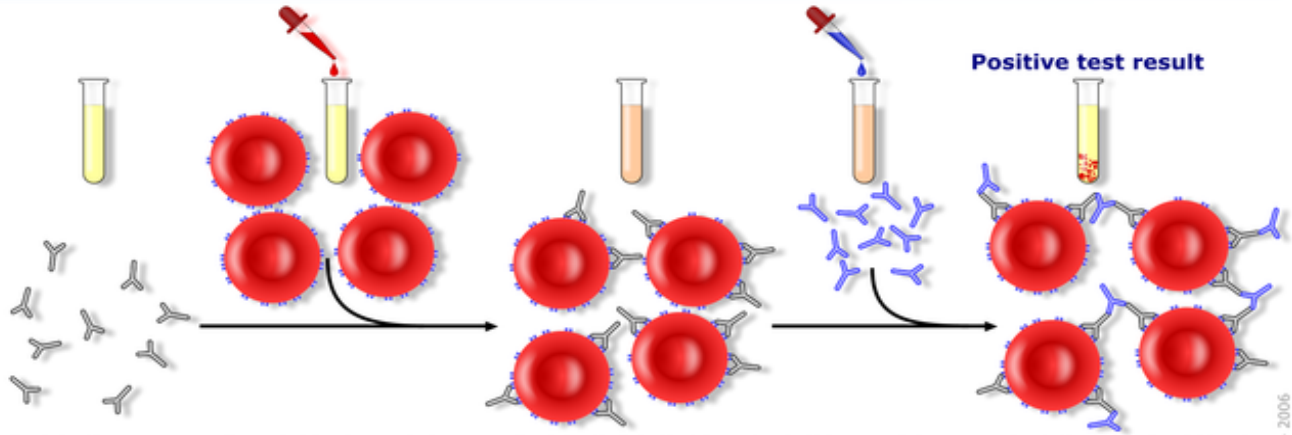


Blood sample from a patient with immune mediated haemolytic anaemia: antibodies are shown attached to antigens on the RBC surface.

The patient's washed RBCs are incubated with antihuman antibodies (*Coombs reagent*).

RBCs agglutinate: antihuman antibodies form links between RBCs by binding to the human antibodies on the RBCs.

Indirect Coombs test / Indirect antiglobulin test



Recipient's serum is obtained, containing antibodies (Ig's).

Donor's blood sample is added to the tube with serum.

Recipient's Ig's that target the donor's red blood cells form antibody-antigen complexes.

Anti-human Ig's (*Coombs antibodies*) are added to the solution.

Agglutination of red blood cells occurs, because human Ig's are attached to red blood cells.

1. Haemolytic Disease

- ➢Jaundice in the first 24 hours of age
- ➢Blood group incompatibility (ABO, Rhesus Less common Kell and Duffy
- ➢Red cell enzyme deficiency
- ➢ Red blood cell membrane defect
- ➢ + ve family history
- ➢ Sepsis (... *poor intake rduce hepatic function and an increase EHC*)

Common MCQ

2. Non-hemolytic N jaundice

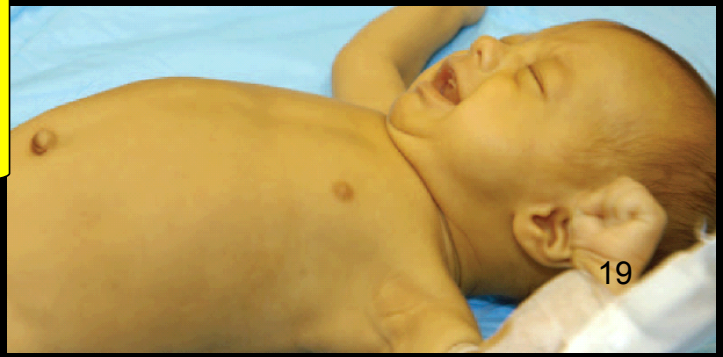
- Increased un-conjugated bilirubin level, normal percentage of reticulocytes or Co

1. Physiologic jaundice Commonest
2. Extra vascular sources
3. Polycythemia
4. Exaggerated Entero- hepatic circulation Obstruction

3- Decreased bilirubin conjugation

1. Physiologic jaundice
2. Crigler-Najjar syndrome
3. Gilbert syndrome
4. Hypothyroidism
5. Breast milk jaundice

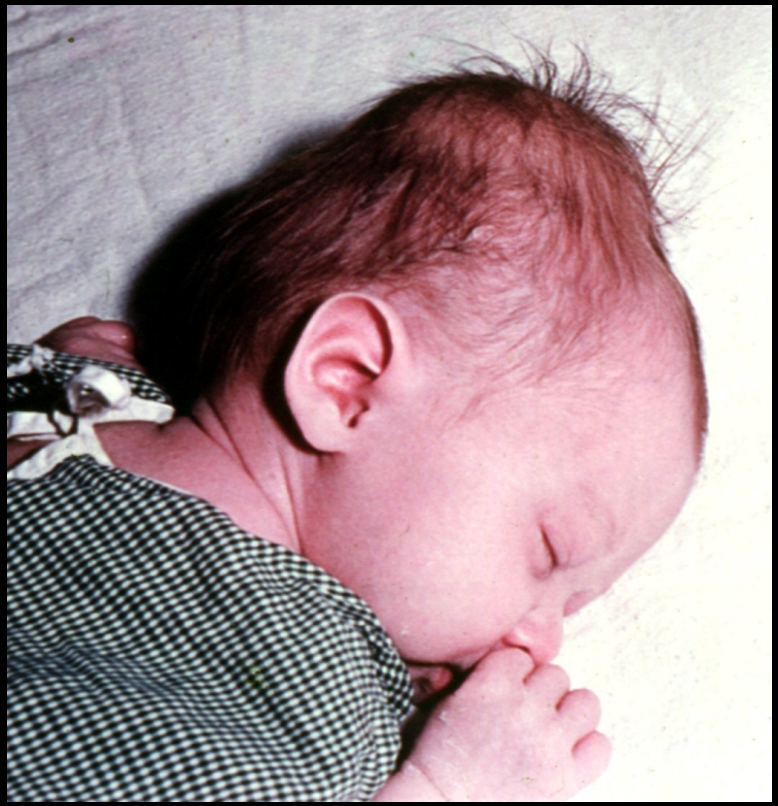
more than 3wk



Cephalic hematoma

Other Ddx :
Caput succedaneuma
Subgaleal hemorrhage

Mcq: Difference between hematoma and succedaneuma



TERM INFANT BORN NSVD DEVELOPED JAUNDICE AT 24 HOURS OF AGE
WHAT IS THE MOST LIKELY CAUSE OF JAUNDICE ?

Soft tissue injuries

These include:

- Caput succedaneum (Fig. 10.4) – bruising and oedema of the presenting part extending beyond the margins of the skull bones; resolves in a few days
- Cephalhaematoma (Figs 10.4, 10.5) – haematoma from bleeding below the periosteum, confined within the margins of the skull sutures. It usually involves the parietal bone. The centre of the haematoma feels soft. It resolves over several weeks

Birth injuries

Soft tissue injuries

- Caput succedaneum, cephalhaematoma, chignon, bruises and abrasions
- Subaponeurotic haemorrhage

Nerve palsies

- Brachial plexus – Erb palsy
- Facial nerve palsy

Fractures

- Clavicle, humerus, femur

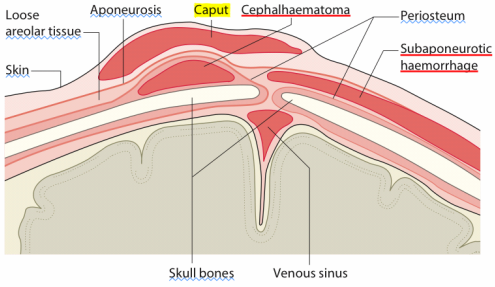


Figure 10.4 Location of extracranial haemorrhages.

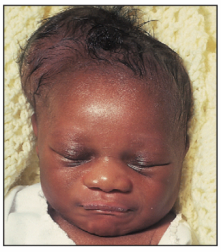


Figure 10.5 A large cephalhaematoma.

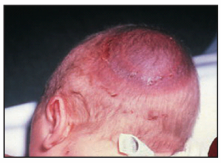


Figure 10.6 Chignon.

Figure 10.7 Erb palsy. The affected arm lies straight, limp and with the hand pronated and the fingers flexed (waiter's tip position).

	nerve	
Caput succedaneum	Diffuse edematous swelling of soft tissues of scalp; **crosses suture lines**	Disappears in first few days; may lead to molding for weeks
Cephalohematoma	Subperiosteal hemorrhage: **does not cross suture lines**	May have underlying linear fracture; resolve in 2 wk to 3 mo; may calcify; jaundice

Cause
Extravascular
hemolysis

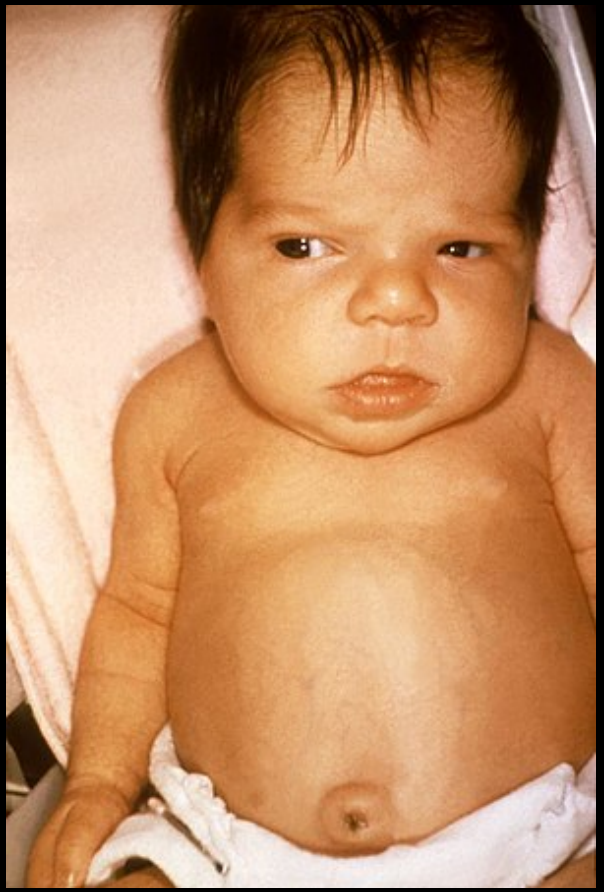
Table 1-2. Common Injuries During Deliveries

6week male infant with prolonged N.J
What is your diagnosis?
How do you manage this infant ?

Hypothyroidism :
Scenario : child comes with jaundice only , and not improved after phototherapy

So its mixed hyperbilirubinemia

Signs of hypothyroidism
- large tongue
- Umbilical hernia



5- ***Impaired bilirubin excretion***
Direct hyperbilirubinemia

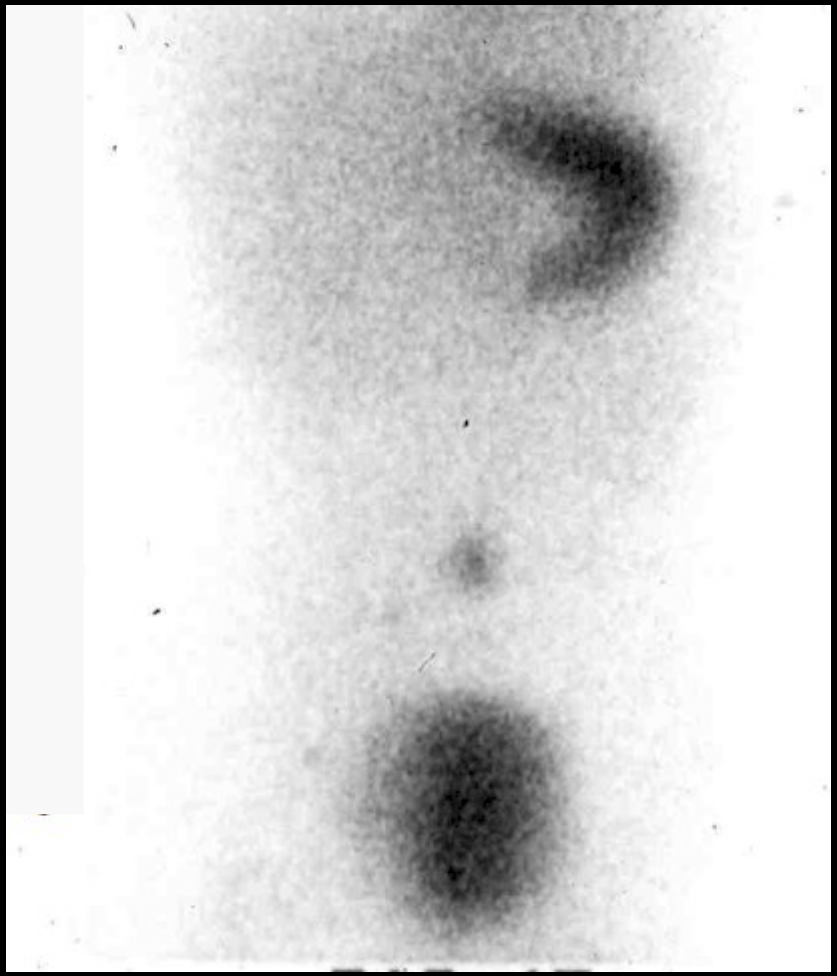
- Conjugated bilirubin level of >2 mg /dL (34 µmol/ L) or >20% of total serum bilirubin level
- Baby passing dark urine and pale stools

1. Biliary obstruction ***(need early promptly DX)***
2. Infection (Hepatitis)
3. Metabolic disorder
4. Chromosomal abnormality

If a baby came with direct hyperbili think about biliary atresia , commonly seen with trisomy 18 (edward syndrome) and trisomy 13 (patau syndrome)

Trisomy 21 (Down syndrome)
If from mother or father its called translocation
If from baby its called nondisjunction

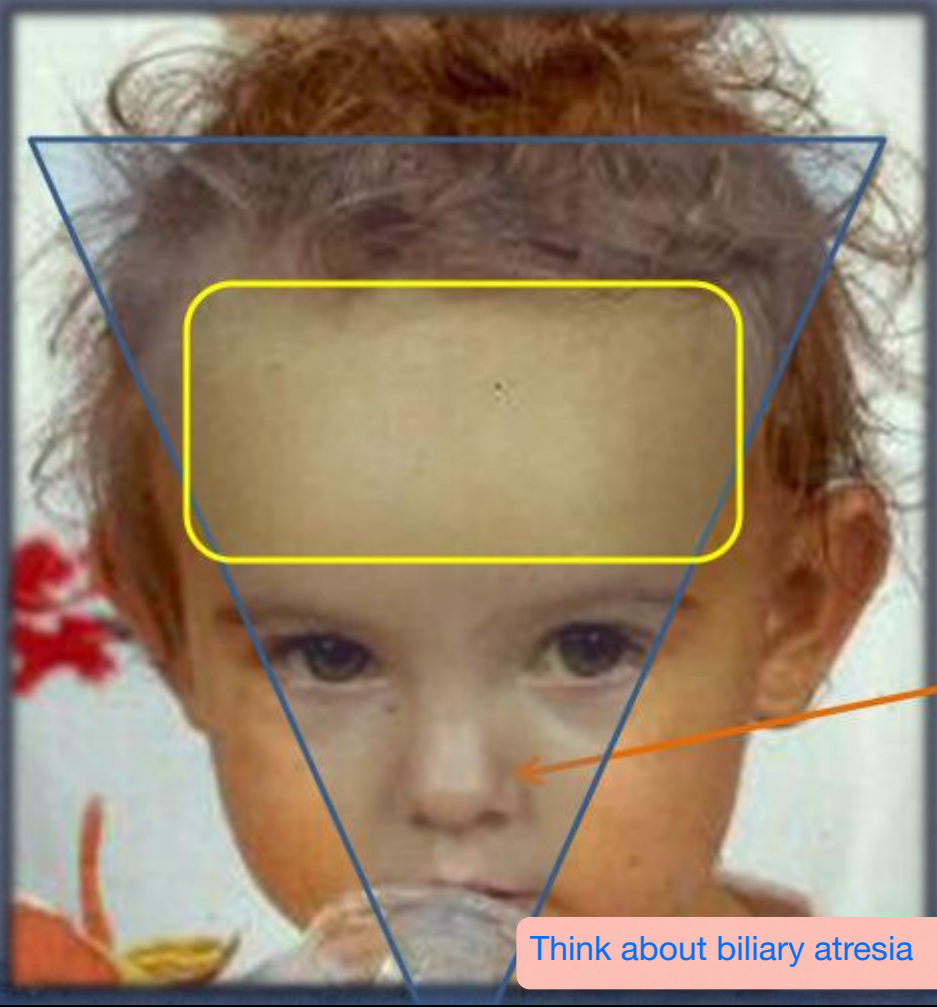
↳ Comments



What is this test?
What is the indication?

HIDA scan to diagnose biliary atresia (not used anymore)

Nowadays they use MRCP



Alagille Syndrome

AD genetic d/o with paucity of bile ducts. May also have PPS and vertebral defects

Features:

- Long nose with bulbous tip
- Triangular face
- Broad forehead

Think about biliary atresia

Case scenario

Term male newborn, presented on the second day of life with jaundice

- Onset (1st or 2nd day)
- Mother blood group
- Symptomatic ? (feeding ? Breast or formula milk ? Active / crying ? Stool/urine color ?

➢What farther questions do you want to obtain?

➢Clinical signs you want to elicit?

➢How do you manage such neonate ?

- CBC (hemolysis -> low Hgb , high reticulocytes)
- check for bilirubin level , direct or indirect ?
- Peripheral blood smear (for spherocytosis and elliptocytosis)
- Use the total serum bilirubin chart/graft
- If the graft shows you the baby at the phototherapy zone then you have to admit the baby.
- > 300 - 400 mg/dl or signs of early kernicterus regardless of bilirubin level then the baby should be admitted to the intensive care unit for exchange transfusion
- If physiologic -> phototherapy

- Yellow skin ? Sclera color ? And jaundice distribution on the trunk (severity)
- Dysmorphic/distinctive features
- Hepatomegaly
- Cardiac defect
- Look at the stool color and urine color yourself

Infants with multiple risk factors may develop an exaggerated form of physiologic jaundice in which the total serum bilirubin level may rise as high as 17 mg per dL (291 μ mol per L)

What is the commonest cause of non hemolytic hyperbilirubineamia?

Physiologic

Criteria for Physiological Jaundice

1. Onset
   - Second day
2. Rate of TSB increment *(5mg/dl/day)*
3. Level of TSB
4. Type of Bili Indirect
5. Duration (Less *than 2wks in term and 3wks in preterm Neonates)*
   - Less than 10 days to 2 weeks if prolonged think about breast milk or hypothyroidism

JAUNDICE AND BREAST FEEDING

- ➢Early-Onset Breast feeding associated Jaundice or Breast feeding failure.
- ➢Breast milk jaundice occurs later in the newborn period usually peaking in the sixth to 14th days of life. Why?

PATHOLOGIC JAUNDICE

All etiologies of jaundice beyond

1) Physiologic
2) breastfeeding or
3) breast milk jaundice

are considered pathologic.

Classification of neonatal jaundice

Physiologic jaundice

- Appears after 24 hours
- Maximum intensity by 4th-5th day in term & 7th day in preterm
- TSB levels within normal centiles for age in hours based on normogram.
- Clinically not detectable after 14 days
- Disappears without any treatment.

Pathologic jaundice

- Appears within 24 hours of age
- Increase of bilirubin > 5 mg / dl / day or at a rate of >0.2mg/dl/hr
- Serum bilirubin >95 percentile for age in hours based on normogram.
- Jaundice persisting after 14 days in fullterm babies.
- Stool clay / white colored and urine staining clothes yellow
- Direct bilirubin> 2 mg / dl or >20% of TSB.

- Phototherapy : it changes the isomerization of the bilirubin
- Illustrated book :Phototherapy : Light (wavelength 450 nm) from the blue–green band of the visible spectrum converts unconjugated bilirubin into a harmless water soluble pigment excreted predominantly in the urine. It is delivered with an overhead light source placed the optimal distance above the infant to achieve high irradiance. Although no long term sequelae of phototherapy from overhead light have been reported, it is disruptive to normal nursing of the infant and should not be used indiscriminately. The infant's eyes are covered, as bright light is uncomfortable. Phototherapy can result in temperature instability as the infant is undressed, a macular rash and bronze discoloration of the skin if the jaundice is conjugated
- Continuous multiple ('intensive') phototherapy is given if the bilirubin is rising rapidly or has reached a high level.

- Distance : almost 35 cm

ABO Incompatibility

- ABO Incompatibility is the most common cause of hemolytic jaundice (10-20%)
- Most ABO antibodies are IgM (some have IgG)
- Commonly Anti A haemolysin occasionally group B
- Coombs positive ABO is more likely to cause hemolysis but less sever then Rhesus
- Hb. is usually normal or slightly reduced
- No hepato-splenomegaly

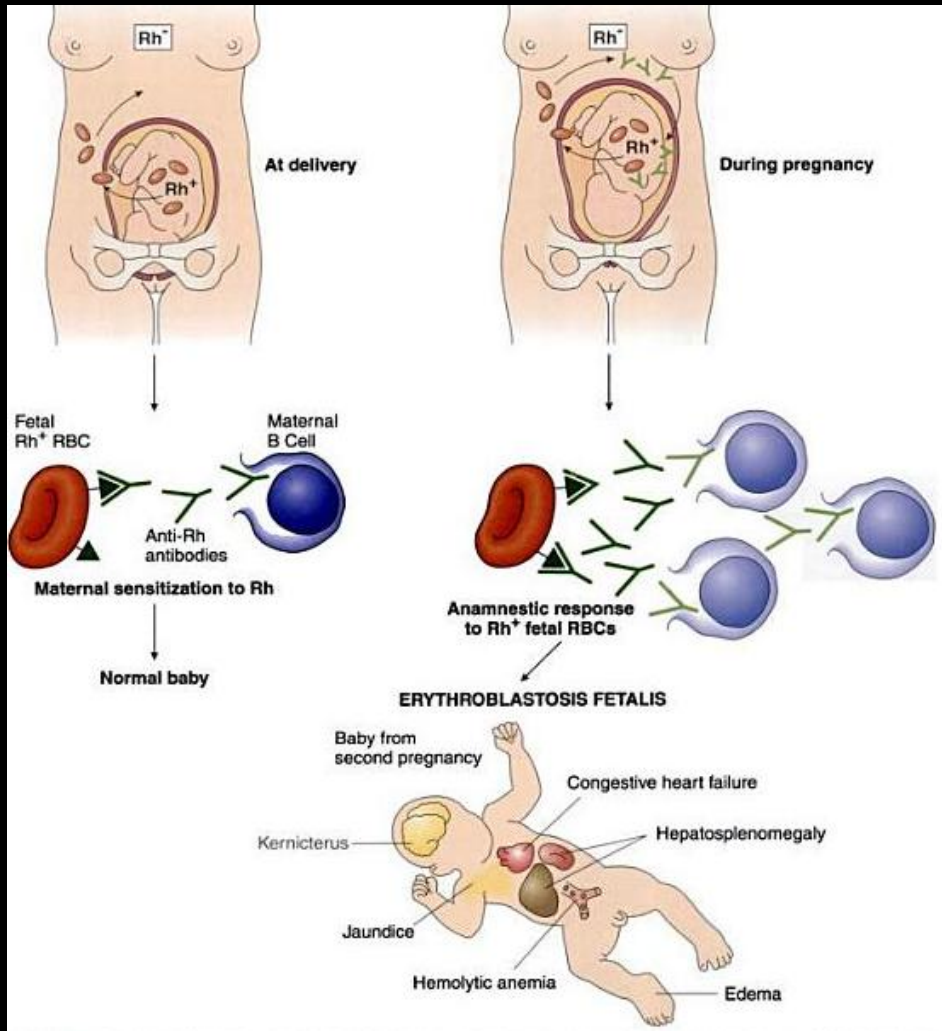
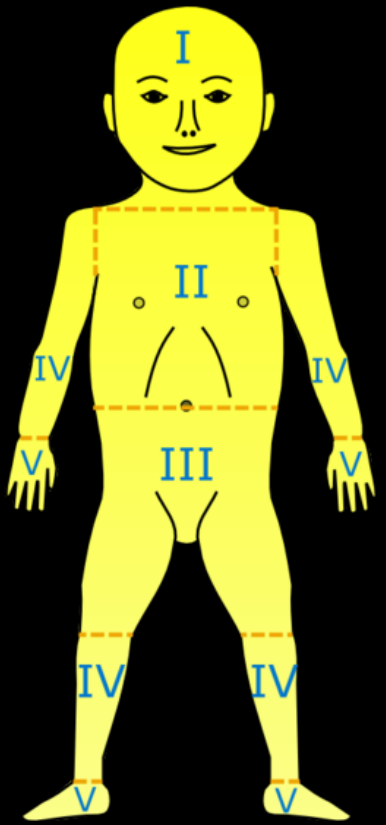
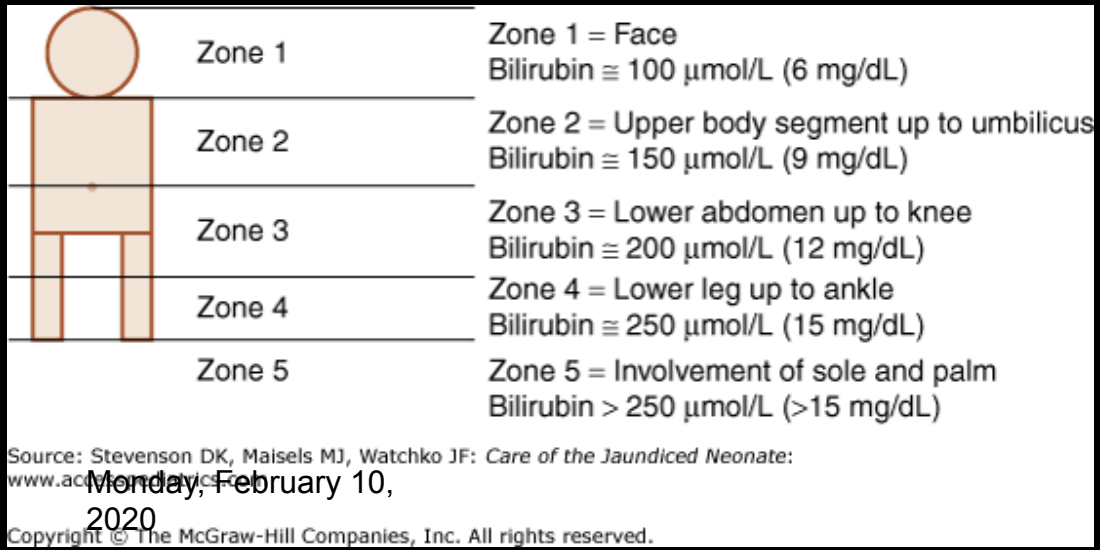


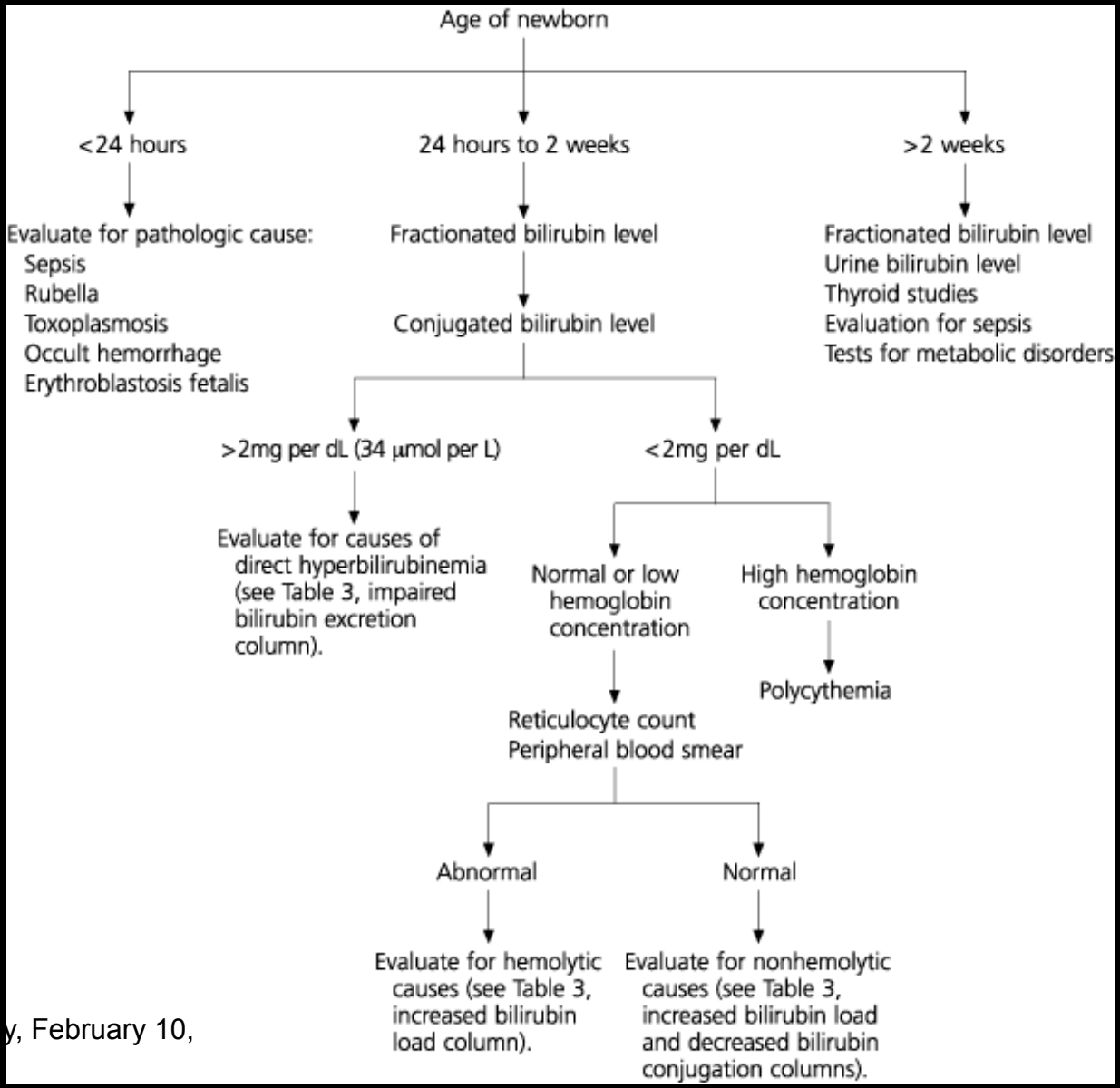
FIGURE 6-42. **Pathogenesis of erythroblastosis fetalis due to maternal–fetal Rh incompatibility.** Immunization of the Rh-negative mother with Rh-positive erythrocytes in the first pregnancy leads to the formation of anti-Rh antibodies of the immunoglobulin (Ig)G type. These antibodies cross the placenta and damage the Rh-positive fetus in subsequent pregnancies.

Diagnosis

- History
- Physical Examination
- Investigation






Age of newborn
<24 hours
24 hours to 2 weeks
>2 weeks
Evaluate for pathologic cause:
Sepsis
Rubella
Toxoplasmosis
Occult hemorrhage
Erythroblastosis fetalis
Fractionated bilirubin level
Conjugated bilirubin level
Fractionated bilirubin level
Urine bilirubin level
Thyroid studies
Evaluation for sepsis
Tests for metabolic disorders
>2mg per dL (34 μmol per L)
<2mg per dL
Evaluate for causes of direct hyperbilirubinemia (see Table 3, impaired bilirubin excretion column).
Normal or low hemoglobin concentration
High hemoglobin concentration
Polycythemia
Reticulocyte count
Peripheral blood smear
Abnormal
Normal
Evaluate for hemolytic causes (see Table 3, increased bilirubin load column).
Evaluate for nonhemolytic causes (see Table 3, increased bilirubin load and decreased bilirubin conjugation columns).

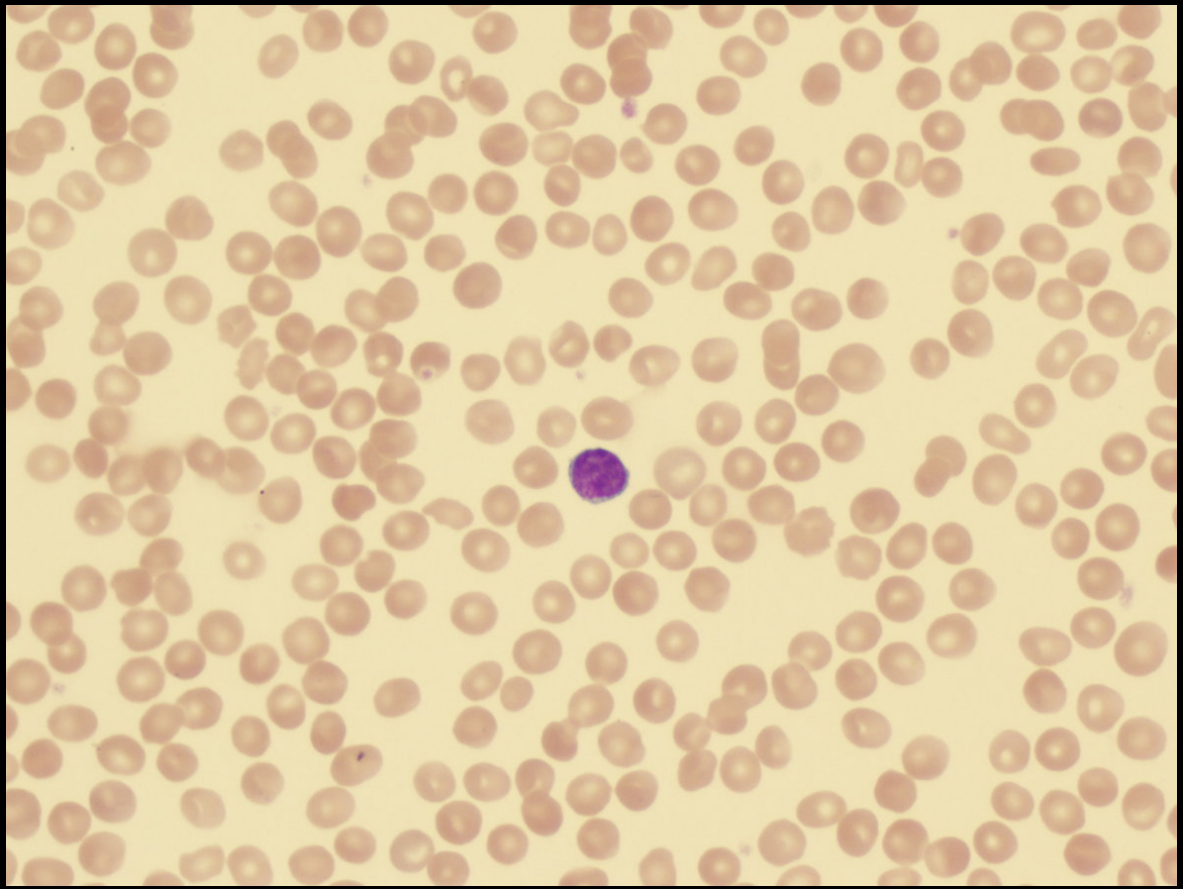
Laboratory Evaluation of Term Newborn with Jaundice

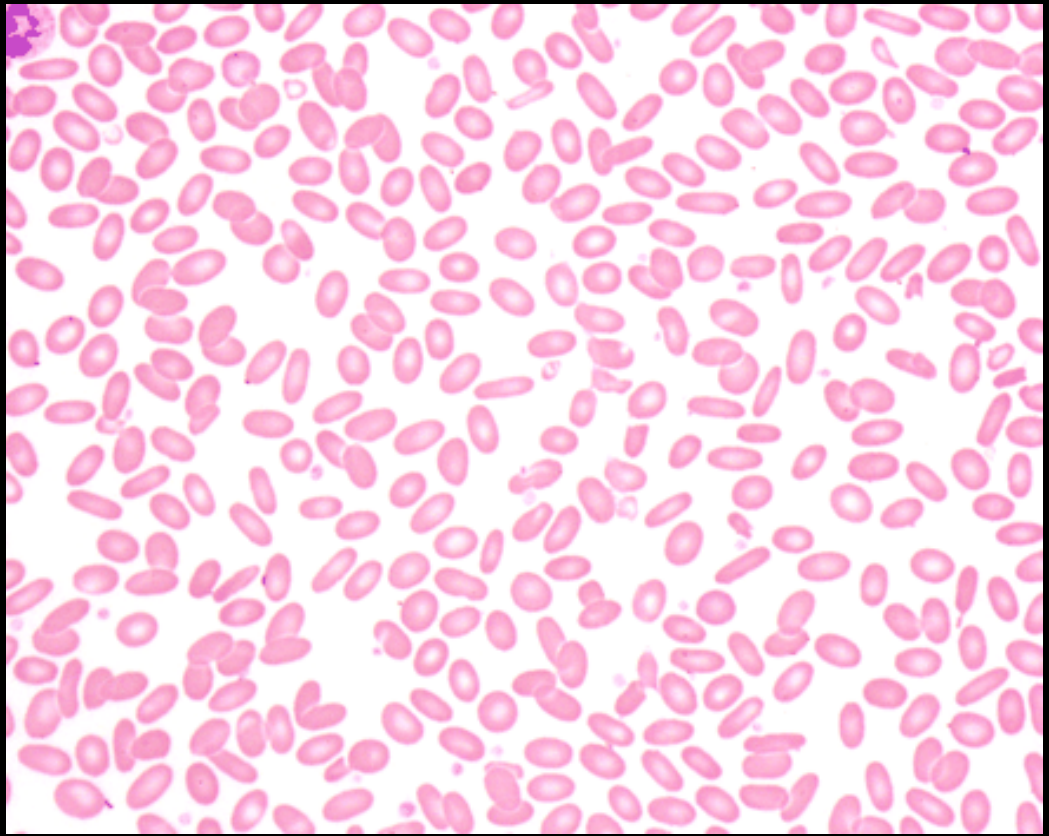
- TOTAL SERUM BILIRUBINE (TSB)
- Bilirubin fraction (conjugated OR non conj.)
- Blood group and comb's test
- CBC. Diff. Retulocytes
- G6PD level
- Peripheral blood smear
- Blood and urine culture **IF** suspected
- Thyroid function & LFT

- What if the lab result shows anemia , reticulocytes zero and everything else is normal ? Do LFTs , check urine and DON'T FORGET G6PD.
- In saudi arabia g6pd enzyme is checked routinely.في بعض المناطق مثل القطيف و جيزان

TRANSCUTANEOUS BILIRUBINOMETER

February 10,





Management

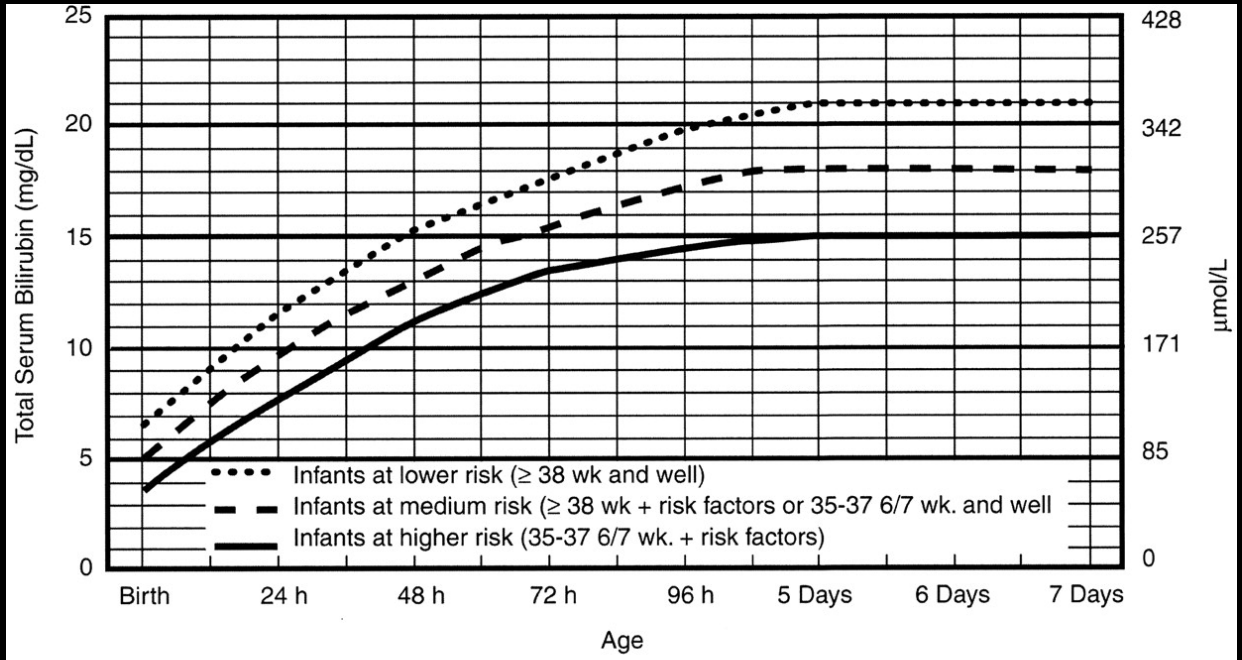
- An increased incidence of kernicterus was found to be associated with total serum bilirubin levels above 20 mg per dL in the presence of hemolysis

✓Hydration And Supportive measures

✓Management guidelines now focus primarily on phototherapy as initial treatment.

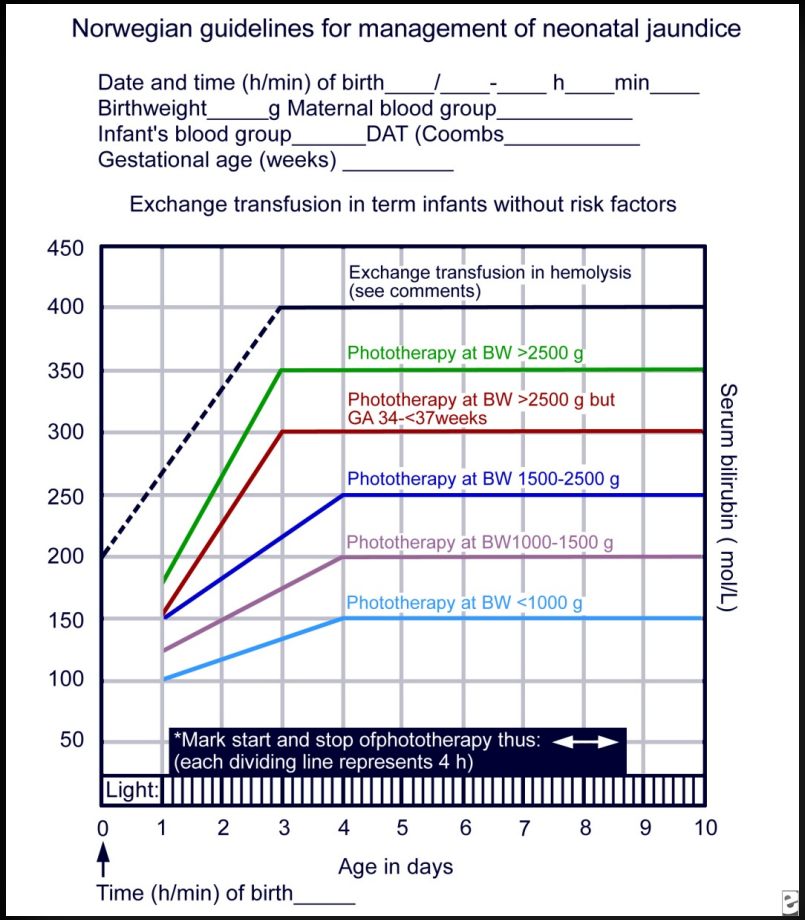
✓Aggressive guidelines recommending the use of exchange transfusion in all infants with significant hyperbilirubinemia

Guidelines for phototherapy in hospitalized infants of 35 or more weeks' gestation

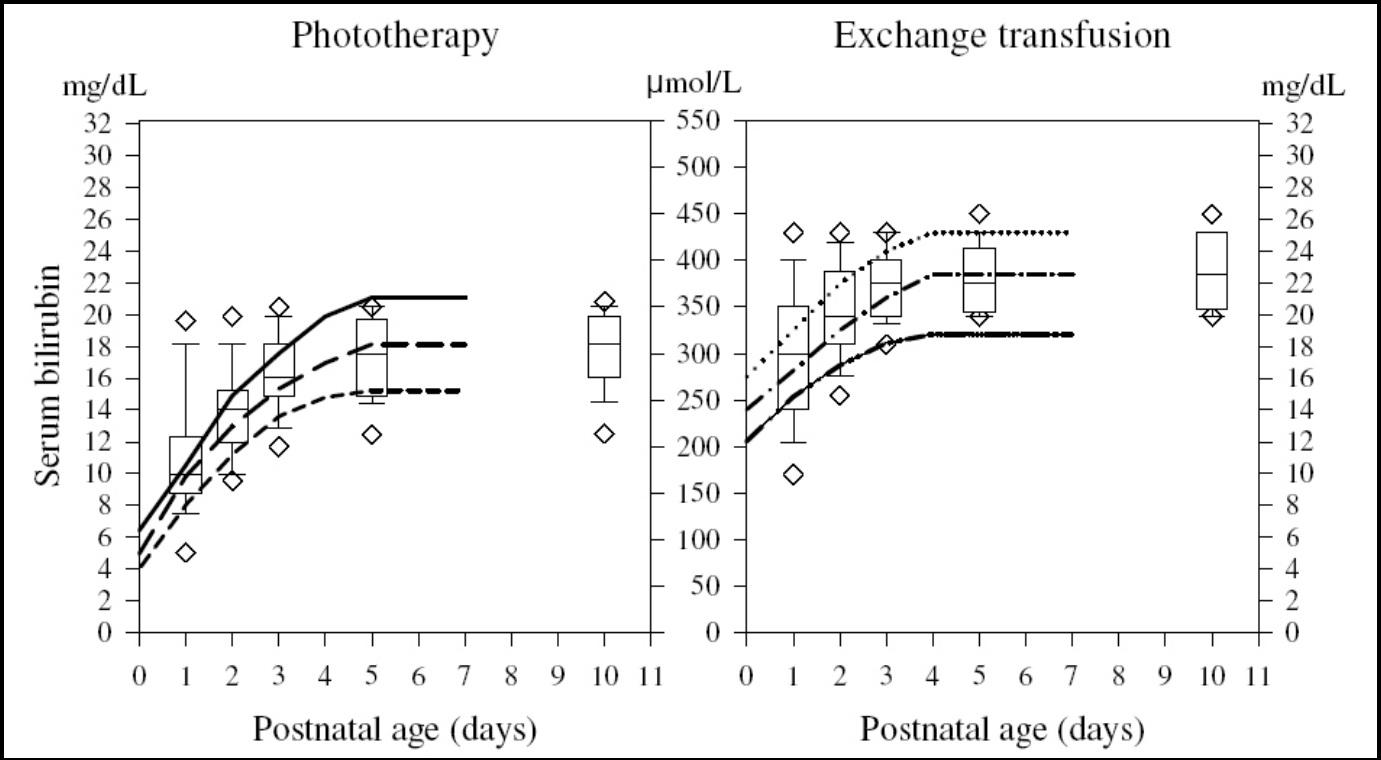


- Use total bilirubin. Do not subtract direct reacting or conjugated bilirubin.
- Risk factors = isoimmune hemolytic disease, G6PD deficiency, asphyxia, significant lethargy, temperature instability, sepsis, acidosis, or albumin < 3.0g/dL (if measured)
- For well infants 35-37 6/7 wk can adjust TSB levels for intervention around the medium risk line. It is an option to intervene at lower TSB levels for infants closer to 35 wks and at higher TSB levels for those closer to 37 6/7 wk.
- It is an option to provide conventional phototherapy in hospital or at home at TSB levels 2-3 mg/dL (35-50mmol/L) below those shown but home phototherapy should not be used in any infant with risk factors.

Guidelines for management



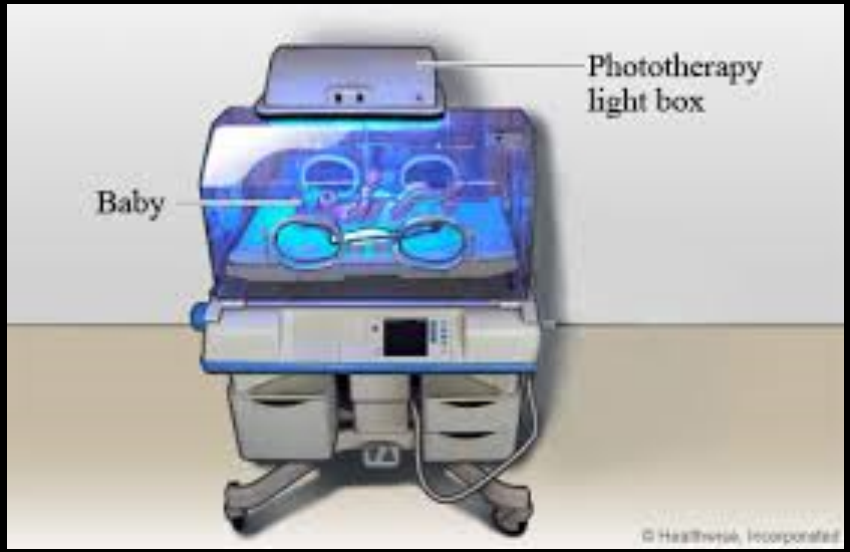
AAP recommendations



PHOTOTHERAPY

light at blue or blue-green wavelengths converts the bilirubin molecule into a form that is either easier to excrete or is less toxic to the neonate
The effective spectrum for this process has been identified *in vitro* to peak at around 450nm (blue light)

PHOTOTHERAPY


Phototherapy
light box
Baby

Conjugated hyperbilirubinemia is never physiologic, and it may indicate the presence of a potentially serious underlying disorder ***HOWEVER***

ELEVATED CONJUGATED BILIRUBIN LEVELS ARE NOT DIRECTLY TOXIC TO BRAIN CELLS IN THE NEONATE.

The therapeutic effect of phototherapy depends on

1. the light energy emitted in the effective range of wavelengths
2. the distance between the lights and the infant
3. the surface area of exposed skin,
4. the rate of hemolysis

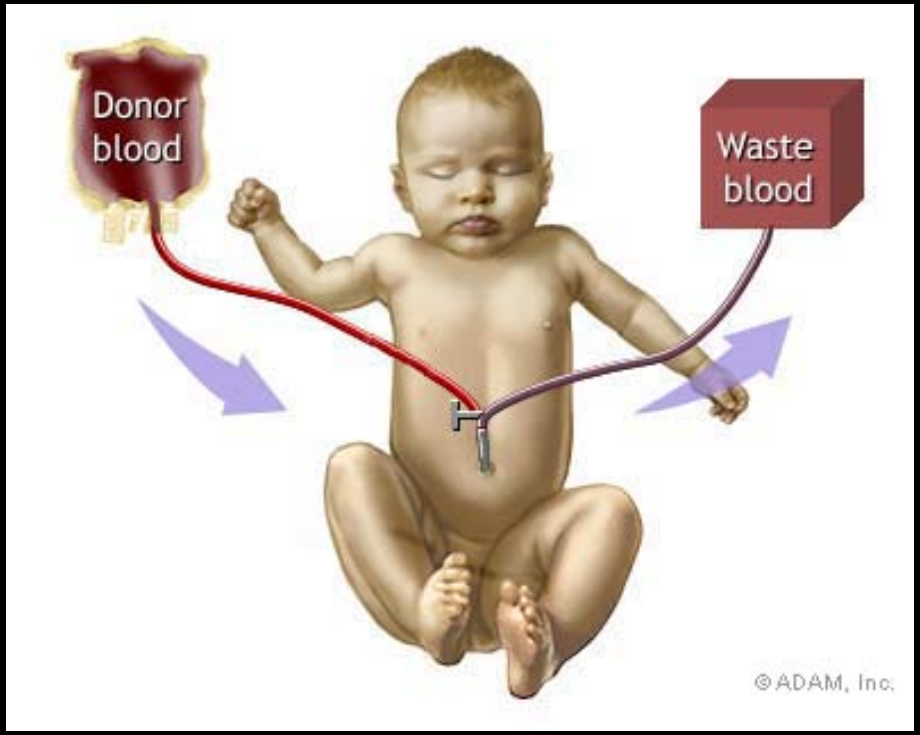
During phototherapy :

1. Cover the eyes and Genitals
2. Supplemental hydration
3. monitoring for side effects
4. Monitering of bilirubin level

Side effects of phototherapy

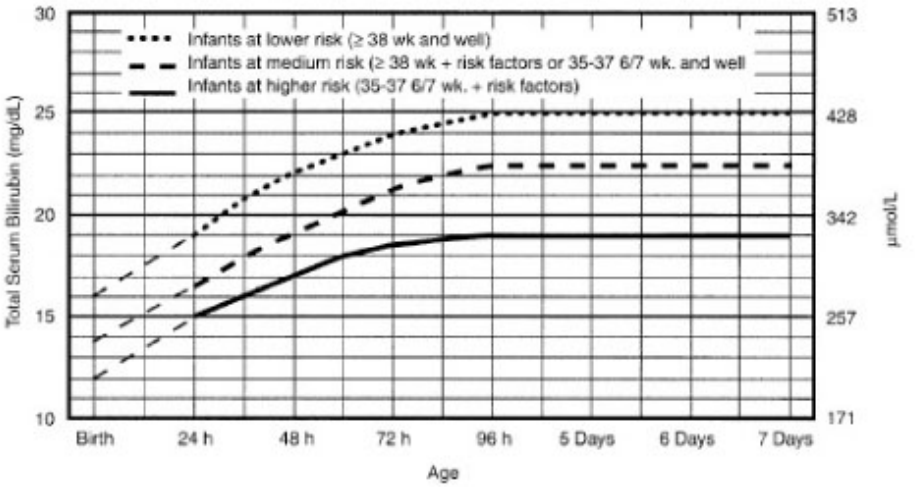
- **Increased insensible water loss**: Frequent Breast feeding.
- **Loose green stools**: weigh often and compensate with breast milk.
- **Skin rashes**: Harmless, no need to discontinue phototherapy.
- **Bronze baby syndrome**: occurs if baby has conjugated hyperbilirubinemia. If so, discontinue phototherapy.
- **Hypo or hyperthermia**: monitor temperature frequently.

EXCHANGE TRANSFUSION



https://youtu.be/ywFFyzjqbJQ
https://youtu.be/0aRHSgBF_Is

EXCHANGE TRANSFUSION

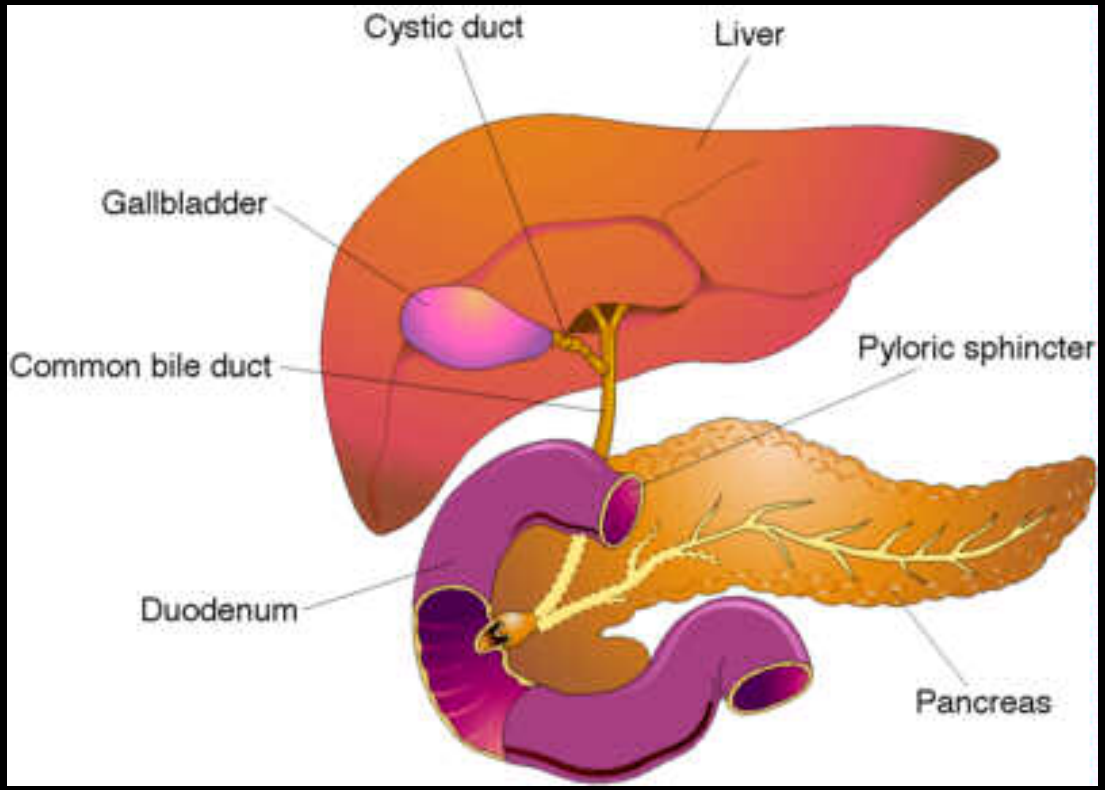


- The dashed lines for the first 24 hours indicate uncertainty due to a wide range of clinical circumstances and a range of responses to phototherapy.
- Immediate exchange transfusion is recommended if infant shows signs of acute bilirubin encephalopathy (hypertonia, arching, retrocollis, opisthotonos, fever, high pitched cry) or if TSB is ≥ 5mg/dL (85 umol/L) above these lines.
- Risk factors = isoimmune hemolytic disease, G6PD deficiency, asphyxia, significant lethargy, temperature instability, sepsis, acidosis
- Measure serum albumin and calculate B/A ratio.
- Use total bilirubin. Do not subtract direct reacting or conjugated bilirubin.
- If infant is well and 35-37 6/7 wk (median risk) can individualize TSB levels for exchange based on actual gestational age.

OTHER

- Immunoglobulin
- Albumin transfusion
- Antibiotics
- Fluid and Electrolytes
- D5% water sun exposure NO
- Phenobarbital ?
- Mesoporphyrin Still under investigation

Conjugated Hyperbili



basal ganglia

hippocampus

Kernicterus

geniculate bodies

cranial nerve nuclei

Pathophysiology

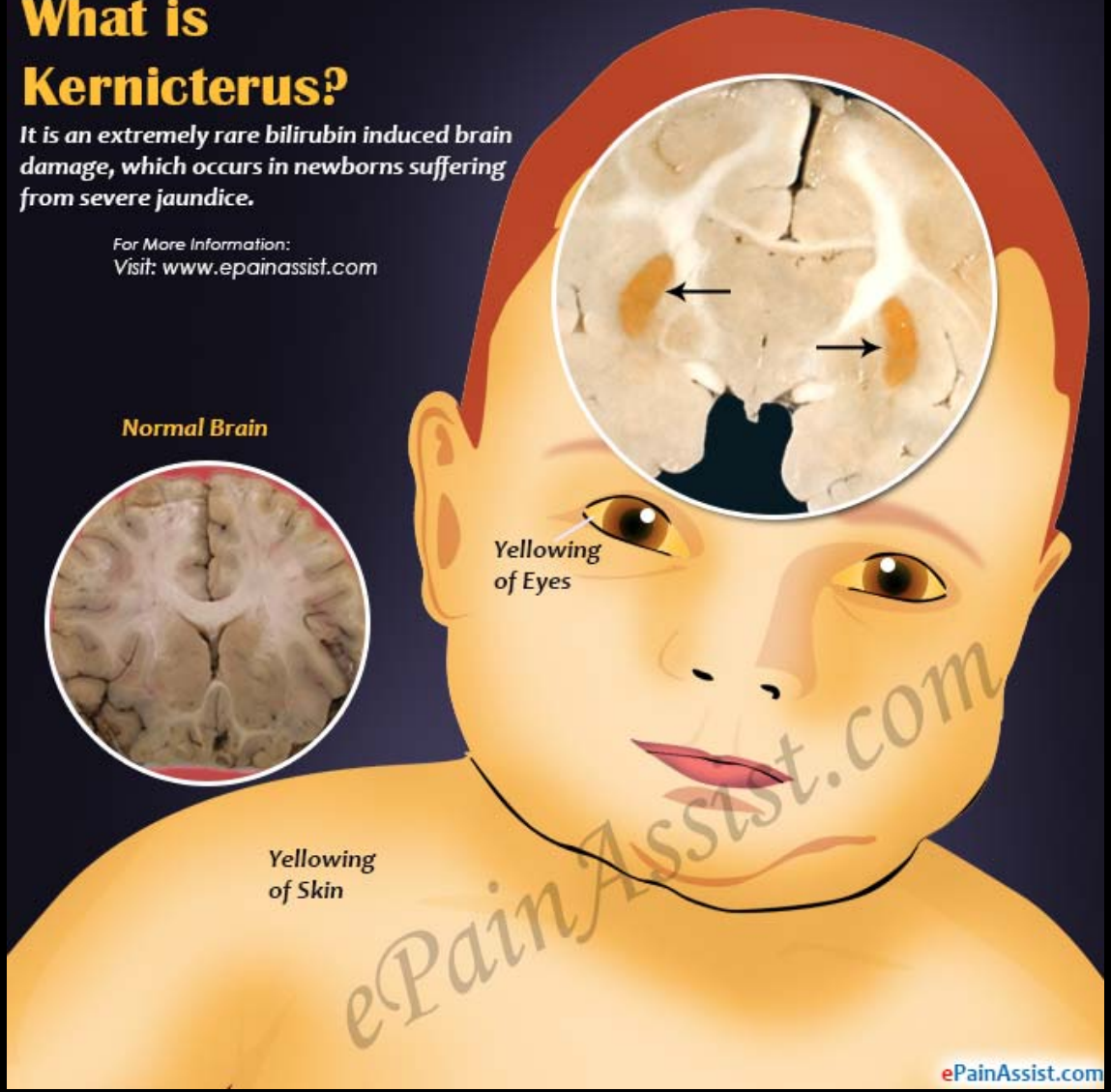
- Bilirubin staining in the regions of the basal ganglia, hippocampus, substantia nigra, and brainstem nuclei
- Staining can occur in the absence of severe hyperbilirubinemia
- Characteristic patterns of neuronal necrosis

ما فيه قيمه معينه للبايلروبين اللي تسبب kernicterus

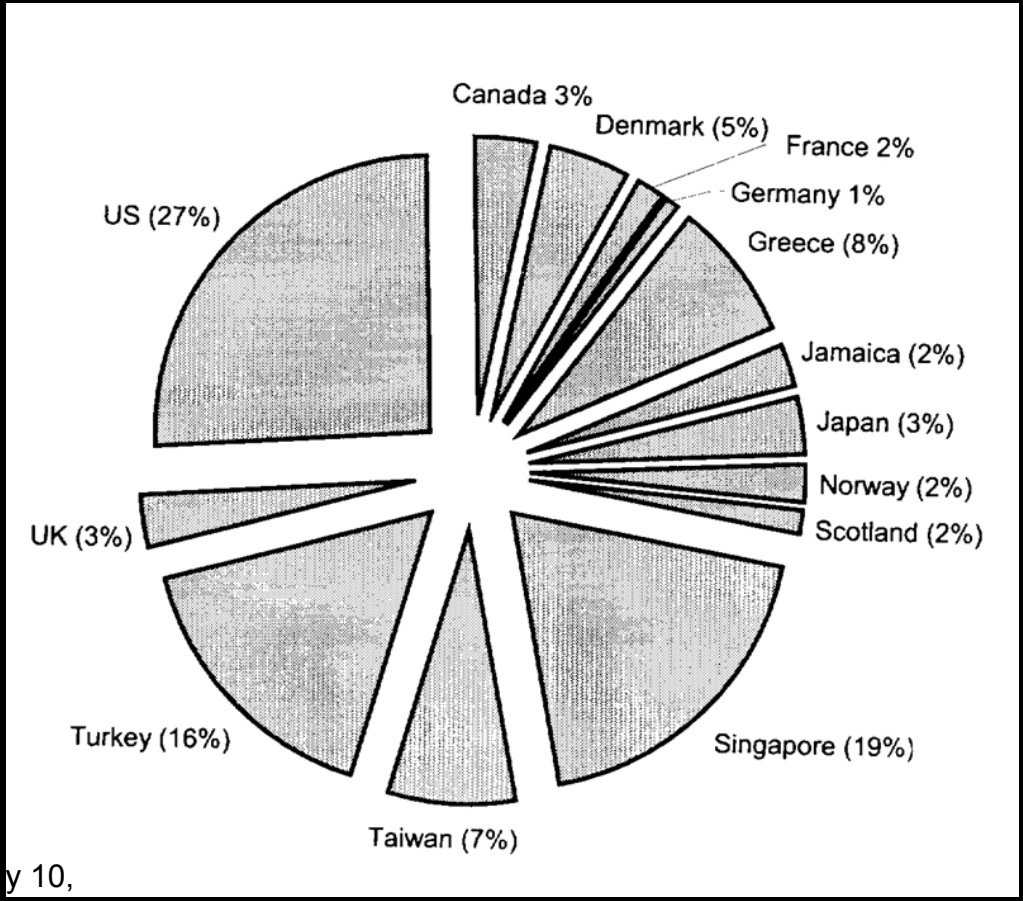
What is Kernicterus?

It is an extremely rare bilirubin induced brain damage, which occurs in newborns suffering from severe jaundice.

For More Information:
Visit: www.epainassist.com



KERNICTERUS



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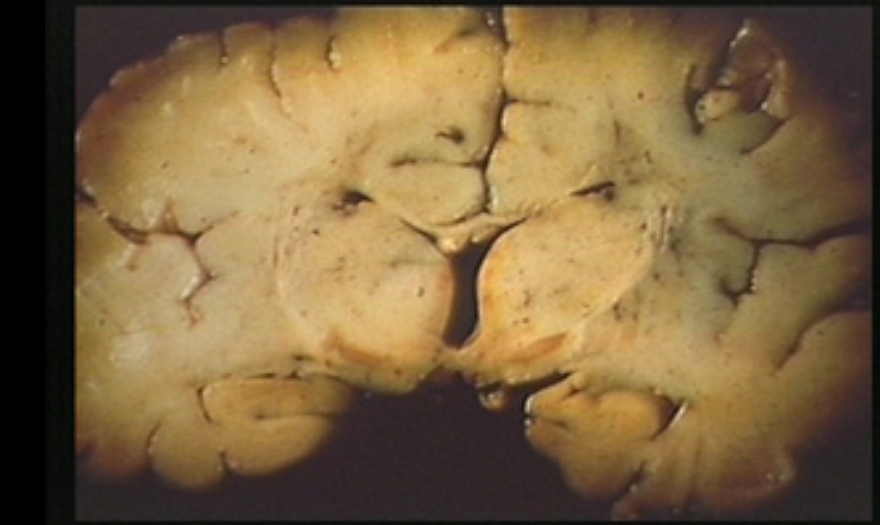
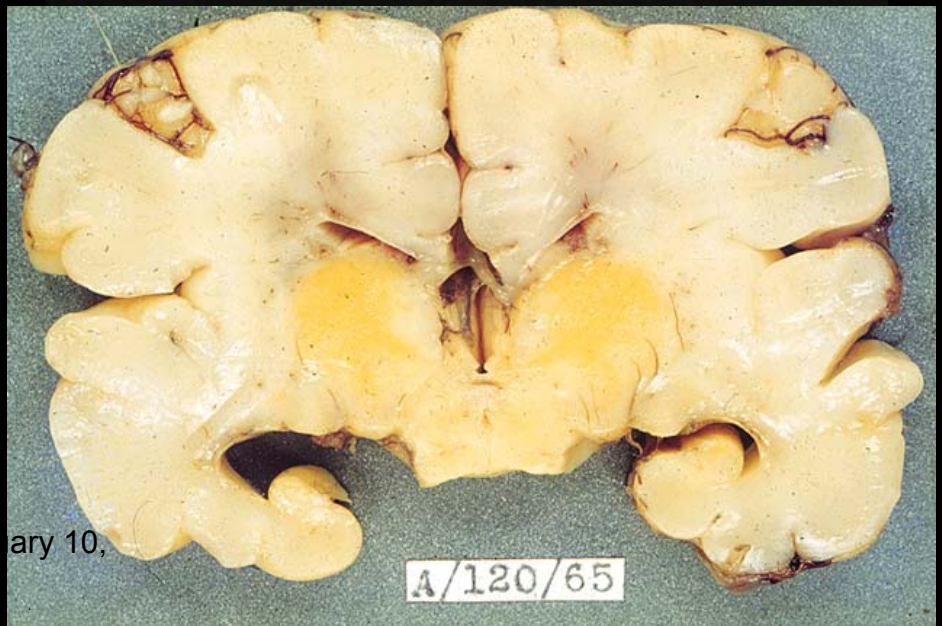




ary 10,

Causes

- Severe hemolytic processes were identified 25%
- Glucose-6-phosphate dehydrogenase (G6PD) deficiency was diagnosed in 22%
- galactosemia occurred in 2.5%
- Crigler-Najjar syndrome type I occurred in
- NO etiology for the severe hyperbilirubinemia was discovered in 73% of cases

Incidence

- Incidence of bilirubin levels >30mg/dl (1/10,000)
- Do we have any registry in Saudi Arabia??
- All reported cases from Saudi literatures were secondary to Crigler Najjarr syndrome

Am J MedGenet. 1998 Aug 27;79(1):12-5

Term Infant with Jaundice

- High pitched cry
- Arching of the baby's body into a bow
- Weakness, limpness, floppiness
- Difficulty nursing and/or sucking

- WHAT IS THE TREATMENT ?

KERNICTERUS

➢Early symptoms-acute bilirubin encephalopathy

✓ poor feeding

✓ abnormal cry

✓ hypotonia,

➢Intermediate phase

✓ -stupor, irritability, hypertonia

➢Late

✓ shrill cry, no feeding, opisthotonus, apnea, seizures, coma, death

Clinical Spectrum: Adverse Effects of Newborn Jaundice

Acute Bilirubin Encephalopathy

Death: respiratory failure

Chronic Post-icteric Sequelae (Kernicterus)

Auditory Neuropathy (isolated)

Subtle manifestations (extra-pyramidal and central posturing disorders) *suspected but not yet proven*

Bilirubin Induced Neurologic Dysfunction (BIND)

KERNICTERUS

➢Late sequelae can include

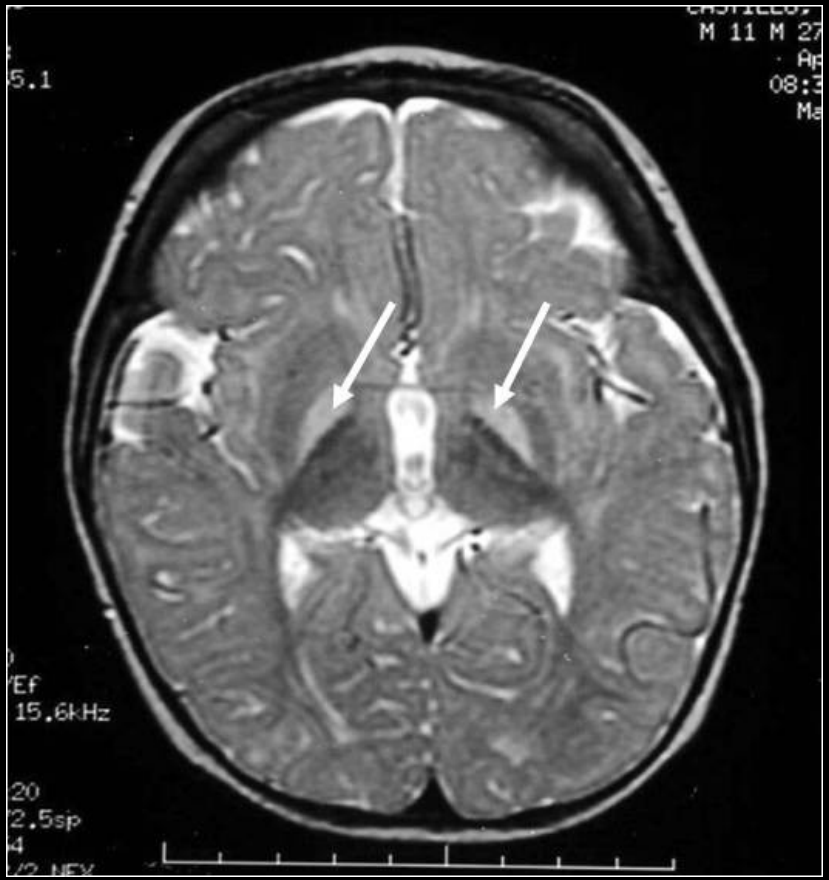
✓ gaze abnormalities
✓ feeding difficulties
✓ dystonia
✓ incoordination
✓ choreoathetosis
✓ sensorineural hearing loss
✓ painful muscle spasms

What is bilirubin level ?

- Over 120 cases kernicterus documented since 1990
- majority term, breastfed
- Majority of those had levels in high 30s to 40s.
- Lowest level recorded in case series of 111 from 1991-2002 was 20.7
- the mean was 38.
- Many cases had no planned follow up and had been discharged early (<48 hours).

Risk Factors

- ASPHYXIA
- ACIDOSIS
- SEPSIS
- HYPOALBUMINEMIA
- YOUNG GESTATIONAL AGE
- LOW BIRTH WT
- HYPERTHERMIA
- RESPIRATORY DISTRESS



Magnetic resonance imaging of the head. Hyperintense basal ganglia lesions on T2-weighted images

Prevention

- Recommend:
  - Promote and support successful breastfeeding.
  - Universal systematic pre-discharge assessment.
  - Provide targeted follow-up based on the risk.
  - Track outcome for timely treatment to prevent excessive hyperbilirubinemia and possibly, kernicterus.

AAP 2004: Recommendations

I. Primary Prevention: lactation support
II. Risk assessment for severe hyperbilirubinemia:
III. Interpretation of TSB values
IV. Cause of jaundice/hyperbilirubinemia.
V. Pre-discharge risk assessment
VI. Hospital policies and procedures
VII. Treatment

Summary

- ➢ Bilirubin physiology
- ➢ Prevent neurotoxicity
- ➢ Identify and treat illness associated with excess production, impaired conjugation or inadequate elimination
- ➢ Combination of therapy

MCQs

A 3-day old full term infant with hemolytic disease of the newborn due to Rh incompatibility has a serum indirect bilirubin concentration of 33 mg/dL. You perform an exchange transfusion with no further elevations of bilirubin above 19 mg/dL. Among the following, the **MOST** appropriate study to use to follow up on this infant is:

A. Another Coomb's test
B. Brainstem auditory evoked response
C. Computed tomography of the head
D. Hemoglobin electrophoresis
E. Indirect retinoscopy

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A. Another Coomb's test
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C. Computed tomography of the head
D. Hemoglobin electrophoresis
E. Indirect retinoscopy

7-day old breastfeed infant born at term has had decreased appetite, irritability and vomiting for 24 hours. On Physical examination, the infant appears listless. Respiratory Rate: 40/min, Heart Rate : 160/min, and blood pressure: 68/38 mm Hg. The skin and sclera are icteric but no other abnormalities noted. Laboratory studies reveal: Hemoglobin: 12 gm/dL. Urinalysis is negative for reducing substances. Of the following, the **MOST** likely diagnosis is:

A. Bacterial sepsis
B. Blood group incompatibility
C. Breast milk jaundice
D. Hypothyroidism
E. Intrauterine infection

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The blood pressure is normal ....
Not hypotensive

A. Bacterial sepsis

B. Blood group incompatibility

C. Breast milk jaundice

D. Hypothyroidism

E. Intrauterine infection

A 3-day old , breast fed infant develops jaundice. The serum bilirubin level is 12 mg/dL with a direct bilirubin component of 0.5 mg/dL. The infant's mother asks whether the jaundice might be associated with breastfeeding. Which of the following statements regarding hyperbilirubinaemia associated with breast feeding is **TRUE:**

A. Indirect hyperbilirubinaemia associated with breast feeding may occur as early as the first day of life.
B. Water supplementation in breast-fed infants will significantly reduce serum concentrations of indirect bilirubin
C. Hyperbilirubinemia associated with breast feeding may persist for 8 to 12 weeks
D. Decreased clearance of bilirubin may play a role in breast feeding jaundice, breast milk jaundice.

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Of the following conditions, which is the **MOST** consistent with findings of mild cholestasis without evidence of biliary atresia?

A. Lead intoxication
B. Chronic hemolytic disease
C. Alpha – antitrypsin deficiency
D. Breast milk jaundice
E. Crigler-Najjar Syndrome

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A 4-week old, breast-fed boy has had mild jaundice since birth. Weight gain has been poor. The urine is light yellow-brown, and the stools are pale yellow-green in color. At this point, the **MOST** appropriate next step in management is to:

A. Observe the child clinically for 2 to 4 weeks
B. Stop breastfeeding and re-examine the child in 7 to 10 days
C. Obtain a cholecystogram
D. Obtain a total and direct serum bilirubin levels and studies of liver function

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You are presenting to 5th year medical student on Neonatal jaundice . Which statement is True ?

A. Is normally excreted in the urine following its conjugation to glucuronic acid

B. Achieve high blood levels due to haemolysis associated with glucose-6-phosphate dehydrogenase deficiency

C. Must be prevented from reaching 340 umol/L in well term babies by use of exchange transfusion if necessary

D. Results from the oxidation of haemoglobin by the enzyme glucuronyl transferase

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Neonatal jaundice is associated with all of the following except :

A. prematurity
B. cystic fibrosis
C. Gilbert's syndrome
D. breast milk feeding
E. neonatal thyrotoxicosis

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A term baby is found to have serum bilirubin of 250 umol/l at 18 hours of age. Which of the following is true?

A. Physiological jaundice is the most likely cause
B. An urgent conjugated bilirubin level is indicated
C. It is unlikely to be due to haemolysis
D. The infants blood group and Coombs test are the most important investigations
E. There is no indication to start phototherapy

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In an infant who appeared healthy at birth, vomiting and diarrhea developed at 1 week of age. She gained weight poorly despite a change from breast milk to infant formula feeding at 2 weeks of age. At 3 weeks of age, she is brought to the emergency department where she is found to be lethargic and to have hepatomegaly. *Of the following, the most likely diagnosis is*

A) Inspissated bile syndrome
B) Crigler-Najjar Syndrome
C) Galactosemia
D) Gilbert Syndrome
E) Dubin-Johnson Syndrome

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6 week old infant presented with early signs of kernicterus. His blood work showed high indirect non hemolytic hyperbilirubinemia. The MOST likely diagnosis :

A. G6PD
B. Physiological Jaundice
C. Crigler Najjer Syndrome
D. Alpha 1 – antitrypsin

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A. G6PD

B. Physiological Jaundice

C. Crigler Najjer Syndrome

D. Alpha 1 – antitrypsin

An apparently term infant who was born at home was noted to be very yellow on the fifth postnatal day. he has no symptoms or clinical signs of bilirubin encephalopathy. His bilirubin concentration is 36.5 mg/dL (624.2 mcmol/L), with a direct bilirubin measurement of 1.5 mg/dL (26.7 mcmol/L). You draw blood to investigate the cause of the hyperbilirubinemia and place the infant under intense phototherapy. Of the following, the MOST appropriate treatment plan is:

A. administration of a bolus of 20 mL/kg normal saline,
B. administration of intravenous fluids with 10% glucose at rate of 150 mL/kg per day
C. administration of salt-poor albumin (1g/kg) over the next hour,
D. initiation of an exchange transfusion as soon as possible

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Thanks for listening

Any Questions ?